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JOYCE VON NATZMER
PEQUIGNOT + MYERS LLC
200 Madison Avenue
Suite 1901
New York, NY 10016

EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,552	WALLUKAT, GERD	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-12,15-25 and 30-38* is/are pending in the application.

4a) Of the above claim(s) *16-25,30,31,33 and 34* is/are withdrawn from consideration.

5)☒ Claim(s) *2-12 and 37-38* is/are allowed.

6)☒ Claim(s) *15,32 and 35-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

Amendment of 9/11/09 has been entered. Claims 2-12, 15-25 And 30-38 are pending. Claims 2-12, 15, 32 and 35-38 are under examination.

OBJECTION(S)/REJECTION(S) OF RECORD WITHDRAWN

The amendment has overcome previously stated issues as follows:

The objection to claim(s) 9, 11 and 32 for informalities.

The objection to claim(s) 10 under 37 CFR 1.75, because claim 10 presently recites “further concentrated”.

The rejection of claim(s) 1 under 35 USC 112, 2nd paragraph for omitting the essential step of returning the precipitated antibodies to their native state. Claim 1 has been cancelled and has been incorporated into claim 6, with the recitation of this essential feature.

The rejection of claim(s) 10 under 35 USC 112, 2nd paragraph.

The rejection of claim(s) 32 and 35 under 35 USC 112, 2nd paragraph for being incomplete.

The rejection of claim(s) 1-15 under 35 USC 112, 1st paragraph for omitting the essential step of returning the precipitated antibodies to their native state after precipitation. Claim 1 has been cancelled and has been incorporated into claim 6, with the recitation of this essential feature.

The prior art rejection of Claims 1-5, 7-10, 15 and 37 under 35 U.S.C. 102(a) or (b) as being entirely anticipated by Wallukat et al (In vitro Cellular…, vol. 38, 376-377,

Jul/Aug 2002)). Claim 6 does not recite “preeclampsia” as one of the diseases associated with detection of the autoantibodies.

The prior art rejection of Claims 12, 32 And 35 under 35 U.S.C. 103(a) as being unpatentable over Wallukat et al al (In vitro Cellular, vol. 38, 376-377, Jul/Aug 2002) in view of Wallukat et al (WO 00/39154). The condition of “preeclampsia” is not within the scope of the diseases associated with detection of the autoantibodies; also, the detection of autoantibodies against peptides having instant SEQ ID NOS:9 and 10 is no longer with the scope of the claims.

NEW REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 9 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 9, line 11 (including line(s) with a strike-through), “in case of malignant hypertension” lacks antecedent basis in claim 6.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential cooperative relationships of the steps, such omission amounting to a gap between the necessary functional relationships. See MPEP § 2172.01. The omitted cooperative relationships are: In claim 11, step i) is recited as a distinct, necessarily further (as now recited in base claim 10) step that is to be conducted before step b) of independent claim 6. However, one of skill in the art would know that preceding precipitation step a) of claim 6 would, like step i) of claim 11, serve as a step of "obtaining an IgG fraction from bodily fluid" (e.g. see Harlow et al (of record) at p 299, for a disclosure of an ammonium sulfate precipitation step); thus, step i) of claim 11 leads to confusion, because it repeats what was already done in step a) of independent claim 6. Furthermore, if one has already conducted step a) of claim 6, then one has necessarily brought a bodily fluid into “contact with an agent for precipitating”; how then could further step i) of claim 11 be conducted with a “bodily fluid”?

MAINTAINED REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant was not in possession of the genus of peptides that have been "modified by means of a deletion, addition and/or substitution."

Since the substitution of a single amino acid within any given parent polypeptide sequence can abolish the binding of an antibody thereto (Lederman et al, Molec. Immunol. 28, 1171-1181, 1991, cited on PTO-892), the use of a peptide other than one having a naturally occurring sequence from "the first and/or second loop" would not likely provide a peptide which would serve as a cognate antigen for detecting disease associated autoantibodies. This position will be maintained irrespective of whether the modification is substitution, or alternatively, a deletion or an insertion. The only possible modification that one of skill could readily envision would be that one could add on flanking residues, such as residues which naturally occur, within the "the first and/or second loop", on one or both sides of an identified epitopic peptide sequence, or such as the residues of a fused tag/flag sequence, or such as a single Cys residue (e.g. for covalently coupling the peptide to a carrier) However, the examiner cannot determine whether applicant has described these kinds of additions. On the other hand, applicant has given the public no direction as to where, within any of the exemplified epitopic peptide sequences, modifications can be made, of any kind, that would permit the peptide to retain its capacity to serve as a cognate antigen for detecting disease associated autoantibodies. One of skill, given any one of the exemplified peptide sequences, thus would not be able to determine which peptides, having one or more modification(s) within their internal sequence, would be members of the genus of useable peptides that would serve as cognate antigens for detecting disease associated autoantibodies.

Applicant's arguments filed 9/11/09 have been fully considered but they are not persuasive. Applicant has argued that he has provided sufficient relevant identifying characteristics of the peptides to be used in the claimed method, such as “partial structures”, “physical and/or chemical properties”, and “functional characteristics coupled with a known or disclosed correlation between structure and function”.

The Office does not consider that the disclosed partial structures give one any idea of what all the modified peptides, within the scope of the claims, might look like. Further, there has been no disclosure of their particular physical/chemical properties, apart from the general physical/chemical properties that would pertain to any peptide. Further, there has been no disclosure of how the functional characteristic of binding to the V-region(s) of naturally occurring autoantibodies is to be correlated with the particularly disclosed and exemplified structures, that have not been modified as in claim 15. That is, there has been no identification of key amino acid residue(s), within any disclosed epitopic sequence, which are essentially present if there is to be any binding to the naturally occurring autoantibodies. One thus does not know which residue(s) could or could not be substituted; one does not know which sub-segment(s) of the disclosed sequences could or could not be disrupted (e.g. by the insertion of an additional amino acid within the sub-segment, or by the deletion of one or more amino acid residues within the sub-segment)

The other arguments presented by applicant, that the level of skill is high, and thus one would know “how to produce the claimed peptides from seed peptides” amounts to an argument that one could conduct an art known process of carrying out further screening for the peptides within the scope of the claim. However, the fact that one who is highly skilled would know how to produce the peptides, after identifying them by a process of screening, does not provide for a proper written description of the identified peptides per se. See Univ. of Rochester…69 USPQ2d 1886.

MAINTAINED/MODIFIED REJECTION(S) UNDER 35 USC 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 32 And 35-36 Are rejected under 35 U.S.C. 102(b) or (e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over either Wallukat et al, (J. Molec. Cell. Cardiol. 1995) or Ronspeck et al (WO 01/21660 or US 6,994,970).

This basis of rejection was previously applied against claims 32 and 35 and has been presently extended to claim 36, which applicant has rendered as an independent claim.

Wallukat et al teach the peptide sequences which constitute the dominant autoantibody-reactive epitopes of the first and second extracellular loops of the β1 adrenoreceptor (andrenegen receptor). These are identical to the peptides having instant SEQ ID NOS: 2 and 3. Wallukat et al note that earlier investigators have shown that the sera of DCM patients contains autoantibodies that react with peptides derived from the first and second extracellular loops of the β1 adrenoreceptor (p 398, col. 2).

Ronspeck et al teach the same epitopic sequences as Wallukat et al, except that Ronspeck et al provide these peptides with flanking sequences derived from the first or second extracellular loops of the β1 adrenoreceptor. Ronspeck et al conduct an ELISA assay for autoantibodies in the sera of DCM patients. See col. 8, lines 11-44. Therein

Ronspeck et al refer to the teachings of Wallukat et al regarding assays. Neither the Wallukat et al nor Ronspeck et al references teach the precise method by which they conducted assays for autoantibodies in the sera of DCM patients. However, the claims do not require any particular immunoassay format, and do not require the use of any particular reagent, except for one or more of the provided peptides. Since each of the references teaches the peptides, claims 32 and 35-36 are anticipated or, at the least, would have been obvious.

Applicant's arguments filed 9/11/09 have been fully considered but they are not persuasive because they point to amendments that have been made which have supposedly taken the claims out of the scope of the prior art. The examiner finds no such changes. The cited prior art was relied upon for teaching SEQ ID NOS:2 and 3, both of which remain in claims 32 and 35, and both of which have been inserted into claim 36. The cited prior art was relied upon for teaching diagnosis of DCM, and the examiner finds that "dilatative cardiomyopathy" remains within the Markush group of diseases recited in claim 32, while claims 35-36 are not limited to the detection of autoantibodies associated with any particular disease.

The added claim limitations concerning the nature of the detection process do not overcome because the prior art has suggested that one would want to detect such autoantibodies, and because any immunoassay for detecting autoantibodies would inherently involve "binding" of the autoantibodies to the peptide, and the "detecting" the autoantibodies that have become "bound" thereto.

FINALITY

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 1/15/10 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644